REMARKS

Claims 1-8, 10-13, 16-23, and 25-26 were pending. Claims 4, 6-8, 10-13, 16-23, and 25-26 stand withdrawn. In the instant amendment, claim 1 has been amended, and new claims 27-40 have been added. Upon entry of the instant amendments, claims 1-3, 5, and 27-40 will be pending and under consideration.

I. AMENDMENTS TO THE CLAIMS

Claim 1 has been amended to recite, in relevant parts, "amino acid sequences which are at least 90% identical to the amino acid sequence shown in SEQ ID NO: 10." Support for the amendments to claim 1 may be found, for example, in the specification at page 9, lines 27-29, as originally filed.

Claims 1 has been amended to delete the term "about" and the phrase "a polynucleotide which represents a fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (d)."

New claim 27 recites "An isolated polynucleotide encoding a RC Kinase polypeptide and being selected from the group consisting of: a) a polynucleotide encoding a RC Kinase polypeptide comprising an amino acid sequence selected from the group consisting of : amino acid sequences which are at least 96% identical to the amino acid sequence shown in SEQ ID NO: 10; and the amino acid sequence shown in SEQ ID NO: 10; b) a polynucleotide comprising the sequence of SEQ ID NO: 4; c) a polynucleotide which hybridizes under stringent conditions to a polynucleotide specified in (a) and (b); and d) a polynucleotide the sequence of which deviates from the polynucleotide sequences specified in (a) to (c) due to the degeneration of the genetic code." Support for new claim 27 may be found, for example, in the specification at page 9, lines 27-29, and claim 1 as originally filed.

New claims 28 and 32 recite an expression vector containing the polynucleotide of claim 27 or 31, respectively. Support for new claims 28 and 32 may be found, for example, in claim 2 as originally filed.

New claims 29 and 33 recite a host cell containing the expression vector of claim 28 or 32, respectively. Support for new claims 29 and 33 may be found, for example, in claim 3 as originally filed.

New claims 30 and 34 recite a method for producing a RC Kinase polypeptide, wherein the method comprises the following steps: a) culturing the host cell of claim 29 or 33, respectively, under conditions suitable for the expression of the RC Kinase polypeptide; and b) recovering the RC Kinase polypeptide from the host cell culture. Support for new claims 30 and 34 may be found, for example, in claim 5 as originally filed.

New claim 31 recites "An isolated polynucleotide encoding a RC Kinase polypeptide and being selected from the group consisting of: a) a polynucleotide encoding a RC Kinase polypeptide consisting of the amino acid sequence shown in SEQ ID NO: 10; b) a polynucleotide consisting of the sequence shown in SEQ ID NO: 4; c) a polynucleotide which hybridizes under stringent conditions to a polynucleotide specified in (a) and (b); and d) a polynucleotide the sequence of which deviates from the polynucleotide sequences specified in (a) to (c) due to the degeneration of the genetic code." Support for new claim 31 may be found, for example, in claim 1 as originally filed.

New claims 35, 37, and 39 recite an isolated antibody that specifically binds to a RC Kinase polypeptide encoded by the polynucleotide of claim 1, 27, or 31, respectively. Support for new claims 35, 37, and 39 may be found, for example, in the specification from page 24, line 9 to page 26, line 18, as originally filed.

New claims 36, 38, and 40 recite the isolated antibody of claim 35, 37, or 39, respectively, wherein the antibody is polyclonal, monoclonal, chimeric, humanized, or single chain. Support for new claims 36, 38, and 40 may be found, for example, in the specification from page 24, line 9 to page 26, line 18, as originally filed.

Applicants respectfully submit that the instant amendments to the claims are fully supported by the application as originally filed and that no new matter is introduced with these amendments. Accordingly, entry of these amendments is respectfully requested.

II. REJECTION OF CLAIMS UNDER 35 U.S.C § 112, FIRST PARAGRAPH FOR LACK OF ENABLEMENT

Claims 1-3 and 5 stand rejected under 35 U.S.C § 112, first paragraph, as allegedly failing to comply with the enablement requirement. The Patent Office alleges that even a single amino acid substitution will often affect the biological activity of a protein. *See* Office Action at page 8. The Patent Office contends that the specification does not provide specific guidance as to the structural elements in the polypeptide encoded by SEQ ID NO: 10 that are

essential for RC Kinase activity, and that one of skill in the art would have to test an essentially infinite number of polynucleotides to determine which ones encode proteins having RC Kinase activity. *See* Office Action at pages 6 and 8. Applicants respectfully traverse the rejection.

Applicants submit that no undue experimentation is required to make or use the claimed subject matter as recited in the amended claims. According to the Court of Appeals for the Federal Circuit, "[t]he specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation.'" *Amgen Inc. v. Hoechst Marion Roussel*, 65 U.S.P.Q.2d 1385, 1400 (Fed. Cir. 2003). Enablement is not precluded by the necessity of experimentation such as routine screening. *See*, *e.g.*, *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988). The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is merely routine, *i.e.*, the key word is "undue," not "experimentation." *Id.* Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 443 F.2d 1386, 1390-91 (C.C.P.A. 1971).

At the outset, Applicants submit that the assays and techniques used to make and use variants of the polynucleotide of SEQ ID NO: 4 and the polypeptide of SEQ ID NO: 10 are routine and well known in the art. Indeed, the Patent Office acknowledges that "enzymatic assays are well known in the art, and the skilled artisan can produce variants of the polynucleotides of SEQ ID NO:[4] or the polypeptide of SEQ ID NO:[10] having the recited structural characteristics using well-known and widely used techniques in the art." *See* Office Action at page 9. The Patent Office alleges, however, that the number of species encompassed by the claims is extremely large and thus the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that a reasonable number of species can be selected for testing. *See id.* The Patent Office alleges that no such guidance is provided in the instant specification. *See id.*

Solely to expedite prosecution, Applicants have amended claim 1 to recite, in relevant parts, "amino acid sequences which are at least 90% identical to the amino acid sequence shown in SEQ ID NO: 10," and to delete the phrase "a polynucleotide which represents a fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (d)."

As such, Applicants submit that independent claim 1, as amended, and dependent claims 2-3 and 5 that incorporate the limitations of claim 1, encompass a reasonable number of species of the presently claimed polynucleotides that can be selected for routine screening.

Further, contrary to the Patent Office's contention, the specification provides considerable guidance and direction with respect to selecting a reasonable number of species for testing, which enables one skilled in the art to practice the claimed subject matter without undue experimentation. For example, the specification discloses that variants and homologs of the disclosed RC Kinase polynucleotides can be identified by hybridization of candidate polynucleotides to known RC Kinase polynucleotides (*e.g.*, SEQ ID NO: 4) under stringent conditions, as is well-known in the art. *See* Specification at page 13, lines 2-5. The specification discloses that candidate variants can be screened from cDNA expression libraries, such as human cDNA expression libraries. *See* Specification at page 13, lines 11-14.

Also, the specification discloses that stringent conditions can be used to obtain and identify variants encoding a RC Kinase polypeptide that are at least 90% identical to SEQ ID NO: 10. For example, by using certain wash conditions, homologous sequences can be identified which contain at most about 5-15% base pair mismatches. *See* Specification at page 13, lines 5-10. The specification further discloses that "it is well known that the T_m of a double-stranded DNA decreases by 1-1.5°C with every 1% decrease in homology (Bonner *et al.*, *J. Mol. Biol.* 81, 123 (1973))." *See* Specification at page 13, lines 14-16. Further, the T_m of a hybrid between a RC Kinase polynucleotide having a coding sequence disclosed herein and a polynucleotide sequence which is at least 90 or 98% identical to that nucleotide sequence can be calculated, for example, using the equation of Boton and McCarthy, *Proc. Natl. Acad. Sci. U.S.A.* 48, 1390 (1962). *See* Specification at page 13, lines 31-34.

In addition, the specification provides a working example, which discloses that RC Kinase activity of a candidate polypeptide can be routinely screened by detecting its phosphorylation of other known RC Kinase polypeptides, MKK4, and MKK6. *See* Specification at page 57. Applicants respectfully submit that enablement is not precluded by the necessity of experimentation such as routine screening. *See*, *e.g.*, *In re Wands*, 858 F.2d at 736-37. Taken together with the disclosure discussed above, the specification provides a reasonable amount of guidance with respect to making and testing a reasonable number of species of polynucleotides encoding a RC Kinase polypeptide comprising amino acid sequences which are at least 90% identical to SEQ ID NO: 10, polynucleotides which

hybridizes under stringent conditions to such polynucleotides, and polynucleotides the sequence of which deviates from such polynucleotide sequences. As such, the presently claimed subject matter does not require a level of ingenuity beyond what is expected from one of ordinary skill in the art. *Fields v. Conover*, 443 F.2d at 1390-91. Given the guidance provided by the specification combined with the knowledge of a skilled artisan, Applicants submit that the presently pending claims are fully enabled as only routine screening would be required to arrive at the presently claimed polynucleotides.

Further, contrary to the Patent Office's contention, Applicants submit that the specification provides reasonable guidance as to the structural elements of a RC Kinase polypeptide. For example, the specification discloses that "Human RC Kinase contains a single S_TKc kinase domain (Serine/Threonine protein kinases, catalytic domain), beginning approximately 268 amino acid residues from the carboxy terminal of SEQ ID NO: 7, 8, 10 or 12 and spanning approximately 256 residues." *See* Specification at page 8, lines 22-24. The specification further discloses that two of the biologically active "variants of Human RC Kinase, SEQ ID NO: 9 and 11, are missing part of this kinase domain." *See* Specification at page 8, lines 25-26. Taken together, the specification provides reasonable guidance that RC Kinase activity at least in part related to the S_TKc kinase domain for its catalytic function, and that the portion of the catalytic domain missing from SEQ ID NOS: 9 and 11 are not necessarily essential for its biologically activity.

Moreover, the specification discloses that biologically active variants, such as SEQ ID NOS: 1-6, retain a RC Kinase activity despite absence of certain exons or portions of certain exons. *See* Specification at page 9, lines 1-12 and 26-27. As such, the specification provides reasonable guidance that certain exons or portions of certain exons are not necessarily essential for RC Kinase activity. In other words, the specification discloses and provides guidance as to which structural regions of a RC Kinase are amenable to sequence variation without losing the biological property a RC Kinase. Therefore, contrary to the Patent Office's contention, 100% homology to SEQ ID NO: 4, or a polynucleotide sequence encoding SEQ ID NO: 10, is not required to retain a RC Kinase activity. Taken together with the enabling disclosure discussed above, Applicants submit that based on the level of skill in the art of generating and identifying variants of the disclosed RC Kinase polynucleotides, it is highly reasonable that one skilled in the art would use a targeted experimental strategy to limit the number of variants to be screened. Such targeted strategies could include, for example, generating variants based on information regarding the structure and function of RC

Kinase, information regarding conserved domains and amino acids, and/or the use of conservative amino acid changes. For at least this reason, Applicants respectfully submit that the specification provides sufficient guidance that enables one of skill to make and use the claimed subject matter in its full scope without undue experimentation.

For at least the foregoing reasons, Applicants respectfully submit that the pending claims are fully enabled. Accordingly, Applicants respectfully request that the rejection of the presently pending claims under 35 U.S.C § 112, first paragraph, be withdrawn.

III. REJECTION OF CLAIMS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Claims 1-3 and 5 stand rejected under 35 U.S.C § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse the rejection.

A. The Legal Standard

The test for sufficiency of written description is whether the disclosure of the application "reasonably conveys to the artisan that the inventor had possession" of the claimed subject matter. *In re Kaslow*, 707 F.2d 1366, 1375 (Fed. Cir. 1983); *accord Vas Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563; *see also, Ralston Purina Co. v. Far Mar Co, Inc.*, 772 F.2d 1570, 1575, 227 (Fed. Cir. 1985). The Court of Appeals for the Federal Circuit has repeatedly considered the written description and consistently found that exacting detail is not necessary to meet the requirement:

If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if not every nuance of the claims is explicitly described in the specification, the adequate written description requirement is met. *In re Alton*, 76 F.3d 1168 (Fed. Cir. 1996). The criteria for determining sufficiency of written description is set forth in Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 T 1, "Written Description Requirement" ("the Guidelines") (published in the January 5, 2001 Federal Register at Volume 66, Number 4, p. 1099-1111), cited with approval in *Enzo Biochem., Inc. v. Gen-Probe, Inc.* (*Enzo II*), 296 F.3d 1316 (Fed. Cir. 2002), specifies that:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see (1)(a) above), reduction to drawings (see

> (1)(b) above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see (1)(c), above). *Id.* at p. 1106, column 3, lines 13-29.

A "representative number" of species is shown where one skilled in the art would recognize that the inventors were in possession of the necessary common attributes or features of the genus claimed. *See Regents of the University of California v. Eli Lilly & Co.*, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). However, each species encompassed within the genus need not be disclosed. *See, e.g., In re Bell*, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993) and *In re Baird*, 29 U.S.P.Q.2d 1550 (Fed. Cir. 1994). Where the specification discloses any relevant identifying characteristics, *i.e.*, functional characteristics coupled with a known or disclosed correlation between function and structure, sufficient to allow a skilled artisan to recognize the applicant was in possession of the claimed invention, a rejection for lack of written description under Section 112, first paragraph, is misplaced. *See* the Guidelines at p. 1106, column 3, lines 13-29.

B. Claims 1-3 and 5 Satisfy the Written Description Requirement

The Patent Office alleges that the specification fails to describe the entire genus of polynucleotides (*i.e.*, fragments, derivatives or variants of SEQ ID NO: 4, or fragments of a polypeptide encoded by SEQ ID NO: 10) when constructed and used as claimed, lacks a written description. *See* Office Action at page 10. The Patent Office further alleges that the breadth of the genus of polynucleotides encoding a RC Kinase that has a homology of at least 75% with SEQ ID NO: 10 and polynucleotides that hybridize to SEQ ID NO: 4 lacks written description. *See* Office Action at page 10. The Patent Office contends that "[a]bsent factual evidence, a nucleic acid having a percentage sequence similarity of less than 100% would not be deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of a similar known biomolecule." *See* Office Action at page 12.

Solely to expedite prosecution, Applicants have amended claim 1 to delete the phrase "a polynucleotide which represents a fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (d)." As such, Applicants submit that the rejection with regard to "fragments or derivatives" is obviated by the amendments to claim 1.

Also, solely to expedite prosecution, Applicants have amended claim 1 to recite, in relevant parts, "amino acid sequences which are at least 90% identical to the amino acid sequence shown in SEQ ID NO: 10." Applicants submit that the specification provides adequate written description for the subject matter in amended independent claim 1, and dependent claims 2-3 and 5 that incorporate the limitations of claim 1.

For one, Applicants submit that the specification provides adequate description as to common identifying characteristics of the claimed polynucleotides, in addition to the sequences of certain polynucleotides species. In particular, the specification discloses structural elements that are in common among the species of the claimed genus of polynucleotides that encode a RC Kinase. For example, the specification discloses that "Human RC Kinase contains a single S_TKc kinase domain (Serine/Threonine protein kinases, catalytic domain), beginning approximately 268 amino acid residues from the carboxy terminal of SEQ ID NO: 7, 8, 10 or 12 and spanning approximately 256 residues." *See* Specification at page 8, lines 22-24. The specification further discloses that two of the biologically active "variants of Human RC Kinase, SEQ ID NO: 9 and 11, are missing part of this kinase domain." *See* Specification at page 8, lines 25-26. Taken together, the specification provides adequate description that RC Kinase activity at least in part is related to the S_TKc kinase domain for its catalytic function, and that the portion of the catalytic domain missing from SEQ ID NOS: 9 and 11 are not necessarily essential for its biologically activity.

Further, as discussed above, the specification discloses that biologically active variants, such as SEQ ID NOS: 1-6, retain a RC Kinase activity despite absence of certain exons or portions of certain exons. *See* Specification at page 9, lines 1-12 and 26-27. As such, the specification provides adequate description that certain exons or portions of certain exons are not necessarily essential for RC Kinase activity. In other words, the specification discloses and provides guidance as to which structural regions of a RC Kinase are amenable to sequence variation without losing the biological property a RC Kinase. Therefore, contrary to the Patent Office's contention, 100% homology to SEQ ID NO: 4, or a polynucleotide sequence encoding SEQ ID NO: 10, is not required to retain a RC Kinase activity. For at least these reasons, Applicants submit that the specification provides a description of the invention describing sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed subject matter of the claims.

With regard to the Patent Office's contention that breadth of the genus of polynucleotides that hybridize to SEQ ID NO: 4 lacks written description, Applicants respectfully submit that claim 1 meets the written description requirement of 35 U.S.C. § 112, first paragraph. For example, claim 1 recites, in relevant parts, "a polynucleotide which hybridizes under stringent conditions to a polynucleotide specified in (a) and (b)." In its *Synopsis of Application of Written Description Guidelines* the Patent Office has provided an "example of genus claims to nucleic acids based on their hybridization properties, and has determined that such claims may be adequately described if they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar." *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 U.S.P.Q.2d 1609, 1615 (Fed. Cir. 2002) (discussing Example 9 on pages 35-37 of *Synopsis of Application of Written Description Guidelines,* available at http://www.uspto.gov/web/menu/written.pdf). Since claim 1 recites polynucleotides that hybridize to SEQ ID NO: 4, or polynucleotides that encode a polypeptide comprising an amino acid sequence which are at least 90% identical to SEQ ID NO: 10 under conditions of high stringency and encode a RC Kinase, which shares common identifying characteristics as discussed above, Applicants respectfully submit that such genus of polynucleotides recited in claim 1 fully meets the written description requirement of 35 U.S.C. § 112, first paragraph.

For at least the foregoing reasons, the present application provides adequate written description support for amended claim 1 and claims 2-3, and 5 that depend from claim 1. Accordingly, Applicant respectfully requests that the rejection of claims 1-3 and 5 under 35 U.S.C § 112, first paragraph, be withdrawn.

IV. REJECTION OF CLAIMS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-3 and 5 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Patent Office alleges that claim 1 recites the phrase "at least about," which is not defined.

Solely to expedite prosecution, Applicants have amended claim 1 to delete the term "about." Applicants submit that the rejection is obviated by the amendments to claim 1.

Accordingly, Applicants respectfully request that the rejections of claims 1-3 and 5 under 35 U.S.C § 112, second paragraph, be withdrawn.

V. REJECTION OF CLAIMS UNDER 35 U.S.C. § 102(b)

Claims 1-3 and 5 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by WO 02/090525 A2 ("'525 publication"). The Patent Office alleges that the '525 publication teaches a polynucleotide sequence SEQ ID NO: 2, which is allegedly 76.4% identical to instant SEQ ID NO: 4 and encodes an amino acid sequence that is allegedly 88.2% identical to the instant SEQ ID NO: 10. *See* Office Action at page 14. The Patent Office further contends that the '525 publication teaches that the polynucleotide can be contained in an expression vector and maintained in a host cell, and that the peptides can be purified from cells that have been altered to express them. *See* Office Action at pages 14-15. Applicants respectfully traverse the rejection.

Solely to expedite prosecution, Applicants have amended claim 1 to recite, in relevant parts, "amino acid sequences which are at least 90% identical to the amino acid sequence shown in SEQ ID NO: 10."

Applicant submits that the '525 publication fails to teach each and every element of independent claim 1, or claims 2-3 and 5 that incorporate every limitation of claim 1. Specifically, the '525 publication does not teach a polynucleotide encoding a RC Kinase polypeptide comprising an amino acid sequence which is at least 90% identical to the amino acid sequence shown in SEQ ID NO: 10 or a polynucleotide comprising the sequence of SEQ ID NO: 4. The '525 publication further does not teach a polynucleotide which hybridizes under stringent conditions to such nucleotides or a polynucleotide the sequence which deviates from the such nucleotide sequences due to the degeneration of the genetic code. For at least these reasons, claims 1-3 and 5 are not anticipated by the '525 publication.

Accordingly, Applicant respectfully requests the rejection of claims 1-3 and 5 under 35 U.S.C. § 102(b) in view of the '525 publication be withdrawn.

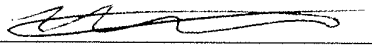
CONCLUSIONS

In light of the above amendments and remarks, the Applicants respectfully request that the Patent Office reconsider this application with a view towards allowance.

No fee is believed to be due with the submission of this paper. However, the Commissioner is authorized to charge all required fees, or credit any overpayment, to Jones Day Deposit Account Number 50-3013 (order no. 191354-999016). The PTO is invited to call the undersigned attorney at (650) 739-3983 if a telephone call could help resolve any issues.

Respectfully submitted,

Date: January 27, 2010



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